oligonucleotide comprising a contiguous stretch of at least about 20 nucleotides of SEQ ID NO:16, as such, claim 10 is definite. Applicants respectfully request that the rejection of claim 10 under 35 U.S.C. § 112, second paragraph, be withdrawn.

## II. THE REJECTION UNDER 35 U.S.C. § 101 IS IN ERROR

Claims 1, 3, 4, and 10 are rejected by the Examiner under 35 U.S.C. § 101 as allegedly lacking patentable utility for the lack of a specific, substantial, and credible utility. Claims 1, 3, 4, and 10 recite oligonucleotides or polynucleotides comprising the disclosed polynucleotide sequences of SEQ ID NOS:9-18. Applicants respectfully traverse the rejection on the ground that such oligonucleotides or polynucleotides have specific, substantial, and credible utilities as described in the specification.

The Examiner states that whether the sequences set forth in SEQ ID NOS:9-18 play a role in the later stages of cellular differentiation and development is a speculation based on the fact that the cells containing such disruptions were viable regardless. The Examiner further alleged that the specification makes no disclosure of evidence disclosing such assertion. Applicants assert that the identified sequences represent a specific class of genes that is involved in late stages of stem cell differentiation and development. These genetic loci encode genetic functions that are not inhibitors of cell death or apoptosis and are not involved in the general survival, *i.e.*, house-keeping functions, of teratocarcinoma cells because one functional allele of these genes does not trigger cell death or apoptosis and that one functional allele of these genes is sufficient for cell survival and growth. The usefulness of such genes is well-established in the art and are described in the originally filed specification, *inter alia*, at page 12, lines 16-24. Support regarding gene function of the presently claimed oligonucleotides and polynucleotides can be derived logically as explained below.

The insertion of a gene trapping vector into a gene will interrupt the proper function of that copy of the gene. If the gene is an inhibitor of cell death or apoptosis and both copies are required for normal function, the cell will die and be lost in a population, and the gene will not be identified by the present invention. If the gene is required for cell viability, this reduction of gene activity by 50% will in most cases result in a decrease in cell viability. Thus, in a population of cells exposed to the gene trapping vectors of the invention, the percentage of cells that can be identified as suffering from a 50% reduction in gene

activity of a gene required for cell viability is disproportionally lower than the percentage of cells that have a 50% reduction in gene activity of a gene not required for cell viability. On the other hand, in the same population, the percentage of cells with an insertion of the gene trap vector in a gene that is not required for cell viability will be higher than the percentage of cells that have a 50% reduction in gene activity of a gene in the genome that are required for cell viability. As the sequences of the invention are derived from the cells with insertions of the gene trap vector, the number of identified genes that are not required for cell viability will be higher compared to the number of identified genes that are required for cell viability. The gene-trapping method of the present invention therefore pre-selects a class of genes that is not involved in cell viability. Genes that are not involved in cell viability are likely to be involved in late stages of stem cell differentiation and development. Thus, the gene trap method enriches a class of genes that is involved in late stages of stem cell differentiation and development.

The gene trap method identifies genes that would not have been identified by conventional forward genetics. By conventional forward genetics, the cells are mutated and selected for an observable phenotype. Subsequently, the mutation is genetically mapped by following the phenotype. Based on the genetic map position, the gene is cloned. Without an observable phenotype, the mutation cannot be genetically mapped and the associated gene cannot be cloned. The gene trap method, in contrast, pre-selects for a class of genes that is not required for cell viability, and thus effectively narrows the scope of the identification process. In other words, the present invention allows one to identify genes that do not have an easily observable phenotype.

The Examiner further alleged that Applicants have not disclose what roles do SEQ ID NOS:9-18 play in the later stages of cellular differentiation and development. Applicants submit that it is not necessary to disclose what such roles are in order to satisfy the specific utility requirement. Applicants submit that since the claimed oligonucleotides or polynucleotides of the present invention is not just any piece of nucleic acid, specific utility requirement has been satisfied. As discussed in the Appeal Brief filed on August 5, 2002, the genetic loci, as represented by the presently claimed oligonucleotides or polynucleotides, which have been disrupted in the teratocarcinoma cells fall within a specific class of genes which is distinct from the broad general class of genes in the genome, as such the present

invention has specific utility. As clearly set forth by the Federal Circuit in *Carl Zeiss Stiftung v. Renishaw PLC*, 20 USPQ2d 1101 (Fed. Cir. 1991):

> An invention need not be the best or only way to accomplish a certain result, and it need only be useful to some extent and in certain applications: "[T]he fact that an invention has only limited utility and is only operable in certain applications is not grounds for finding a lack of utility." *Envirotech Corp. v. Al George, Inc.*, 221 USPQ 473, 480 (Fed. Cir. 1984)

Just because the Applicants have not disclose what precise biological roles do the presently claimed polynucleotides or oligonucleotides have in the later stages of cellular differentiation and development does not mean that the presently described polynucleotides or oligonucleotides lack utility.

In addition, Applicants submit that the claimed oligonucleotides and polynucleotides are specifically identified and functionally validated exons (*i.e.*, exons which had been actually spliced during post-transcriptional processing) that would not have been identified by conventional molecular biology approaches. Exhibit C shows the sequence alignments of SEQ ID NOS:9-18 with human genomic sequences in GenBank. As set forth in the specification, *inter alia*, at page 12, line 12, the present invention provides tools for identifying exon splice junction, chromosome mapping, etc. This is precisely the utility of the present invention as set forth throughout the specification as originally filed. The specification, *inter alia*, at page 20, lines 12-15, describes that the claimed oligonucleotides or polynucleotides from the intron/exon boundaries of the human gene can be used to design primers for use in amplification assays to detect mutations within the exons, introns, splice sites (e.g., splice acceptor and/or donor sites) that can be used in diagnostics. For example, as shown in Exhibit C, Applicants submit that SEQ ID NO:16 defines a coding region since SEQ ID NO:16 spans four distinct exons on chromosome 22 (bases 90259 to 90085; bases 90631 to 90504; bases 89080 to 89014; and bases 94134 to 94085 from Genbank accession number AL021391 which is a clone from chromosome 22) that are separated by introns (bases 89081 to 90084; bases 90260 to 90503; and bases 90632 to 94084 from Genbank accession number AL021391).

Applicants point out that only a small percentage (2-4%) of the human genome actually encodes exon sequences, and these exons are widely interspersed within a given chromosome. When the gene comprising these exons are expressed, the cell must clip out these exons and assemble them end-to-end in order to produce a functional mRNA which

acts as a template for the translation of a protein product. The claimed oligonucleotides or polynucleotides comprising the sequence of SEQ ID NOS:9-18 encode exons that are actually spliced together to produce an active functional transcript (*i.e.*, one of the utilities of the described sequences is for defining intron/exon splice-junctions). Exon splice junctions are particularly important in the study of disease and cancer because splice junctions can often be hot spots for erroneous events leading to these disease states. Applicants respectfully submit that the practical scientific value of biologically validated, expressed, spliced, and polyadenylated mRNA sequences is readily apparent to those skilled in the relevant biological and biochemical arts.

For further evidence in support of the Applicants' position, the Examiner is requested to review, for example, section 3 of Venter *et al.*, 2001, Science 291:1304 (Exhibit D) particularly Fig. 11 at pp.1324-1325, which demonstrates the significance of expressed sequence information in the structural analysis of genomic data. The present polynucleotide sequence defines a biologically validated sequence that provides a unique and specific resource for mapping the genome essentially as described in the Venter *et al.* article. In disclosing a functionally validated exon splice junction, the claimed oligonucleotides or polynucleotides provide physical evidence that effectively trumps the hypothetical conclusions provided by bioinformatics analysis of the corresponding genomic region conducted without supporting physical data. Thus, the present sequence clearly meets the requirements of 35 U.S.C. § 101.

Furthermore, the gene trapped sequences of the present invention overcome some of the limitations of conventional cDNA and expressed sequence tag libraries. In particular, the claimed oligonucleotides or polynucleotides were identified using gene trap vectors that are independent of the level of endogenous mRNA expression of a gene for identification of that gene. The gene trap vectors are able to trap poorly expressed genes.

Still further, Applicants point out that each of the sequences of the present invention can be used to map a specific region on a specific human chromosome. The specificity of each of the claimed oligonucleotides or polynucleotides are listed below: SEQ ID NO:9 can be used to map a specific region of human chromosome 5, due to the fact that SEQ ID NO:9 aligns with two clones from chromosome 5 (Genbank accession numbers AC012640 and AC034241); SEQ ID NO:10 can be used to map a specific region of human chromosome 12, due to the fact that SEQ ID NO:10 aligns with a clone from chromosome 12

(Genbank accession number AC140062); SEQ ID NO:11 can be used to map a specific region of human chromosome 4, due to the fact that SEQ ID NO:11 aligns with a clone from chromosome 4 (Genbank accession number AC112518); SEQ ID NO:12 can be used to map a specific region of human chromosome 9, due to the fact that SEQ ID NO:12 aligns with a clone from chromosome 9 (Genbank accession number AL158207); SEQ ID NO:13 can be used to map a specific region of human chromosome 10, due to the fact that SEQ ID NO:13 aligns with a clone from chromosome 10 (Genbank accession number AL161936); SEQ ID NO:14 can be used to map a specific region of human chromosome 11, due to the fact that SEQ ID NO:14 aligns with a clone from chromosome 11 (Genbank accession numbers AC092768); SEQ ID NO:15 can be used to map a specific region of human chromosome 12, due to the fact that SEQ ID NO:15 aligns with a clone from chromosome 12 (Genbank accession number AC008115); SEQ ID NO:16 can be used to map a specific region of human chromosome 22, due to the fact that SEQ ID NO:16 aligns with a clone from chromosome 22 (Genbank accession number AL021391); SEQ ID NO:17 can be used to map a specific region of human chromosome 18, due to the fact that SEQ ID NO:17 aligns with a clone from chromosome 18 (Genbank accession number AC015933); SEQ ID NO:18 can be used to map a specific region of human chromosome 1, due to the fact that SEQ ID NO:18 aligns with a clone from chromosome 1 (Genbank accession number AL360270). Exhibit C shows the sequence alignments of SEQ ID NOS:9-18 with Genbank human genomic sequences. The presently claimed oligonucleotides or polynucleotides have specific utility in mapping the protein encoding regions of the corresponding human chromosome, as described in the specification, *inter alia*, at page 12, line 12. The exquisite specificity of each of the claimed oligonucleotides or polynucleotides for their specific locus on a corresponding human chromosome is evidenced by the fact that each of the claimed oligonucleotides or polynucleotides do not specifically align with any other human genomic sequences. Hence, the claimed polynucleotides are not random fragments of genomic DNA of unknown location. Thus, the present sequence clearly meets the utility requirements of 35 U.S.C. § 101.

While earlier mapping techniques have identified gross chromosomal positions for numerous disease-associated genes, these techniques are inadequate to precisely map these genes. However, using the presently described nucleotide sequence and a computer system, the exact location of such disease-associated genes is able to be specifically pinpointed, as detailed above. The claimed oligonucleotides or polynucleotides provide

exquisite specificity in localizing the specific region of a particular human chromosome that contains the gene encoding the given polynucleotide, a utility not shared by virtually any other nucleic acid sequences. In fact, it is this specificity that makes this particular sequence so useful. Early gene mapping techniques relied on methods such as Giemsa staining to identify regions of chromosomes. However, such techniques produced genetic maps with a resolution of only 5 to 10 megabases, far too low to be of much help in identifying specific genes involved in disease. The skilled artisan readily appreciates the significant benefit afforded by markers that map a specific locus of the human genome, such as the present oligonucleotides or polynucleotides.

The Examiner further states that the claimed sequences do not have a substantial utility because the sequences are not "refined and developed to this point-where specific benefit exists in currently available form," requiring further experimentation of a skilled practitioner. In response, Applicants respectfully point out that the pre-selected class of genes have currently available utility in the characterization of important regulators of cell differentiation. For example, the sequences identified by the gene trap method can be used to assemble a micro-array or gene chip. When the micro-array or gene chip is hybridized with RNA from teratocarcinoma cells of different differentiation stages, genes that are involved in the differentiation of this type of cells and their relative expressive levels are determined. Using a micro-array or gene chip with genes that are pre-selected for their involvement in differentiation and development reduces the number of genes that need to be screened as compared to a micro-array of genes randomly picked from a genome sequence database. Gene chips clearly have utility, as evidenced by many issued U.S. Patents, as exemplified by U.S. Patent Nos. 5,445,934, 5,556,752, 5,744,305, 5,837,832, 6,156,501 and 6,261,776. Given the widespread utility of such methods using gene sequence information, there can be little doubt that the use of the presently described oligonucleotides or polynucleotides would have great utility in such gene chip applications. Clearly, there can be no doubt that the skilled artisan would know how to use the presently claimed oligonucltides or polynucleotides. As the present oligonucleotides or polynucleotides are specific markers of the human genome, and such specific markers are targets for the discovery of drugs that are associated with human disease, those of skill in the art would instantly recognize that the present nucleotide sequence would be an ideal, novel candidate for assessing gene expression using such gene chips. Clearly, compositions that enhance the utility of such gene chips,

such as the presently claimed nucleotide sequence, must in themselves be useful. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

Further, the claimed oligonucleotides or polynucleotides of the invention provide the skilled artisan with probes to isolate the full length cDNA of the genes represented by the sequences of the invention without undue experimentation. The full length cDNAs can be obtained by cDNA library screening with the sequences of the invention. The sequences of those genes are useful for identifying polymorphisms in coding regions and associating those polymorphisms with disorders. For the reasons set forth above, those genes are pre-selected for genes involved in cell differentiation; they can, therefore, be used for developing therapies for disorders involving abnormal cell differentiation.

The Examiner further alleged that the claimed oligonucleotides can only be used to further study (or to determine) the genes to which they hybridize to. As such, Applicants clearly have not arrived at the "successful conclusion" of what the actual function of the gene is or how such gene is involved in the development and differentiation of teratocarcinomas. Applicants submit that these genetic loci as represented by the presently claimed nucleic acids have substantial utility not because they can be used to do further research, they have substantial utility because hybridization of a nucleic acid allow inference to useful information; they provide useful information regarding gene expression in teratocarcinoma cells which mimics gene expression during the late stages of stem cell differentiation and development. As such, the claimed oilgonucleotides and polynucleotides have substantial utility.

Evidence of the "real world" substantial utility of the present invention is further provided by the fact that there is an entire industry established based on the use of gene sequences or fragments from genes in a gene chip format. Perhaps the most notable gene chip company is Affymetrix. However, there are many companies which have, at one time or another, concentrated on the use of gene sequences or fragments, in gene chip and non-gene chip formats, for example: Gene Logic, ABI-Perkin-Elmer, HySeq and Incyte. In addition, two such companies (Agilent acquired by American Home Products and Rosetta acquired by Merck) were viewed to have such "real world" value that they were acquired by large pharmaceutical companies for significant sums of money. The "real world" substantial industrial utility of gene sequences or fragments would, therefore, appear to be widespread and well established. Furthermore, compositions that enhance the utility of such DNA chips

by specifically identifying biologically validated expressed nucleotide sequences, such as the presently claimed sequence, must in themselves be useful. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

Applicants respectfully point out that the Utility Guidelines provide that, in evaluating evidence related to utility, the character and amount of evidence needed to support an asserted utility will vary depending on what is claimed and whether the asserted utility appears to contravene established scientific principles and beliefs. For the claimed utility to be credible, the invention must be "believable based on the record or the nature of the invention" (M.P.E.P. 2107.02(III)(A). Applicants assert that because of the nature of the invention and for the reasons set forth above, the sequences of the invention which are pre-selected for sequences representing genes that are involved in the differentiation and development of teratocarcinoma cells have credible utility.

Applicants submit that the above described utilities are well known in the art, and hence utilities of the present invention are credible. As stated in the Examination Guidelines for the Utility Requirement, credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure or any other evidence of record (66 FR 1098, Jan 5, 2001). Accordingly, not only do the oligonucleotides and polynucleotides of the present invention have specific utilities, their utilities are credible and practical.

In view of the foregoing, Applicants submit that the claimed inventions have specific, substantial and credible utility.

## III. THE REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH SHOULD BE WITHDRAWN

Claims 1, 3, 4, and 10 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking utility.

The Federal Circuit and its predecessor have determined that the utility requirement of Section 101 and the how to use requirement of Section 112, first paragraph, have the same basis – the disclosure of a credible utility. *See In re Brana*, 51 F.3d 1560, 1564, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995); *see also In re Jolles*, 628 F.2d 1322, 1326 n. 11, 206 USPQ 885, 889 n. 11 (CCPA 1980); and *In re Fouche*, 439 F.2d 1237, 1243, 169 USPQ 429, 434 (CCPA 1971).

Applicants traverse this rejection on the ground that Claims 1, 3, 4, and 10 have significant patentable utility as discussed in Section II, above. Applicants submit that when an Applicant satisfactorily rebuts a rejection based on a lack of utility under 35 U.S.C. § 101, the corresponding rejection imposed under 35 U.S.C. § 112, first paragraph, should also be withdrawn. Thus, Applicants respectfully request that the rejection of Claims 1, 3, 4, and 10 under 35 U.S.C. § 112, first paragraph, be withdrawn.

Claims 1, 3, 4, and 10 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification. The Examiner contended that the specification lacks written description of the claimed nucleic acids because the claimed sequence reads on 1) a synthetic oligonucleotide that is a full-length cDNA or 2) a full-length cDNA which hybridizes to the claimed oligonucleotides.

According to 35 U.S.C. § 112, first paragraph, an applicant must convey with reasonably clarity to those skilled in the art that the applicant was in possession of the invention. *Vas-Cath v. Mahurkar*, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). An adequate description of a chemical genus requires a precise definition by *structure, formula, chemical name* or *physical properties* sufficient to distinguish the genus from other materials. *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). The standard for claims involving chemical materials has been explicitly stated by the Federal Circuit:

> In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. *Univ. of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Thus, a claim describing a genus of nucleic acid by *structure, formula, chemical name* sufficient to distinguish the genus from other materials meets the written description requirement of 35 U.S.C. § 112, first paragraph. By virtue of the sequences recited in claims 1, 3, 4, and 10, the claimed isolated oligonucleotides and polynucleotides are fully described by *structure*, sufficient to distinguish the claimed isolated oligonucleotides and polynucleotides from other materials.

Claim 1 recites an oligonucleotide that comprises a contiguous stretch of at least about 30 nucleotides of at least one of SEQ ID NOS:9, 10, 12, 13, 17, and 18. Thus, one of skill in the art can readily distinguish the isolated oligonucleotide of claim 1 from other materials by the description provided in claim 1. Whether a particular nucleic acid sequence comprises 30 contiguous nucleotides of at least one of SEQ ID NOS:9, 10, 12, 13, 17, and 18 can be determined by the skilled artisan by sequence analysis.

Merely because the sequences may contain sequences in addition to at least about 30 contiguous nucleotides of at least one of SEQ ID NOS:9, 10, 12, 13, 17, and 18, the claim should not be rejected for lack of written description. Here, the new aspect of the claimed isolated polynucleotides is the stretch of at least about 30 contiguous nucleotides of at least one of SEQ ID NOS:9, 10, 12, 13, 17, and 18, which is unambiguously described in the application by virtue of the sequence listing. Applicants submit that the written description requirement for the claimed genus of molecules are met.

In view of the foregoing, Applicants respectfully request that the rejection of Claims 1, 3, 4, and 10 under 35 U.S.C. § 112, first paragraph, be withdrawn.

## IV. THE REJECTIONS UNDER 35 U.S.C. § 102(b) SHOULD BE WITHDRAWN

Claim 1 is rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Duncan *et al.*, (EP 505605-A, September 1992) ("Duncan *et al*"). The Examiner states that Duncan *et al.* discloses a nucleic acid sequence which comprises 15 contiguous nucleotide sequence to that of SEQ ID NO:9. Applicants have amended claim 1 to recite an oligonucleotide that comprises a contiguous stretch of at least about 30 nucleotides of at least one of SEQ ID NOS:9, 10, 12, 13, 17, and 18. As such, Applicants submit that Duncan et al. does not teach or suggest Claim 1. Applicants request that the rejection of Claim 1 under 35 U.S.C. § 102(b) is obviated and should be withdrawn.

Claims 1 and 3 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Zhao *et al.*, (GenBank Accession Number AQ534984, direct submission 1997) ("Zhao *et al*"). The Examiner states that Zhao *et al.* discloses a nucleic acid sequence which comprises 112 contiguous nucleotide sequence to that of SEQ ID NO:15. As discussed above, Applicants have amended claim 1 to recite an oligonucleotide that comprises a contiguous stretch of at least about 30 nucleotides of at least one of SEQ ID NOS:9, 10, 12,

13, 17, and 18. Applicants have also amended claim 3 to recite an isolated polynucleotide comprising a contiguous stretch of at least 60 nucleotides of at least one of SEQ ID NOS:9, 10, 12, 13, 14, and 16-18. As such, Applicants submit that Zhao et al. does not teach or suggest Claims 1 or 3. Applicants have also added new claim 12 to recite an isolated polynucleotide consisting essentially of a contiguous stretch of at least about 125 nucleotides of SEQ ID NO:11 or 15. Applicants request that the rejection of Claims 1 or 3 under 35 U.S.C. § 102(b) are obviated and should be withdrawn.

Claim 1 is rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Kaushansky (WO 95/21626-A1, August 17, 1995)("Kaushansky"). The Examiner states that Kaushansky discloses a nucleic acid sequence which comprises 21 contiguous nucleotide sequence to that of SEQ ID NO:18. As discussed above, Applicants have amended claim 1 to recite an oligonucleotide that comprises a contiguous stretch of at least about 30 nucleotides of at least one of SEQ ID NOS:9, 10, 12, 13, 17, and 18. As such, Applicants submit that Kaushansky does not teach or suggest Claim 1 and thus the rejection of Claim 1 under 35 U.S.C. § 102(b) is obviated and should be withdrawn.

## CONCLUSION

Applicants submit that Claims 1, 3, 4, 10, and 12 satisfy all of the criteria for patentability and are in condition for allowance. An early indication of the same and passage of Claims 1, 3, 4, 10, and 12 to issuance is therefore kindly solicited.

Respectfully submitted,

Date: April 7, 2003

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## Exhibit A

## Marked-Up Version of Amended Claims

1. (Three Times Amended) An oligonucleotide comprising a contiguous stretch of at least about [15] 30 nucleotides of at least one of SEQ ID NOS:[9-13, 15,] 9, 10, 12, 13, 17, and 18.

3. (Three Times Amended) An isolated polynucleotide comprising a contiguous stretch of at least about 60 nucleotides of at least one of SEQ ID NOS: [9-18] 9, 10, 12, 13, 14, and 16-18.

10. (Twice Amended) [A synthetic] An oligonucleotide comprising a contiguous stretch of at least about 20 nucleotides of [at least one of SEQ ID NOS] SEQ ID NO:16.

11. (Canceled) [An isolated polynucleotide capable of hybridizing to a polynucleotide or an oligonucleotide of Claim 1, 3, 4, or 5 under high stringency conditions comprising incubating at 65°C in 0.5M $NaHP0_4$, 7% sodium dodecyl sulfate (SDS), 1mM EDTA and washing at 68°C in 0.1xSSC and 0.1% SDS.]

12. (New) An isolated polynucleotide consisting essentially of a contiguous stretch of at least about 125 nucleotides of SEQ ID NO:11 or 15.

## Exhibit B

## Pending Claims

1. (Three Times Amended) An oligonucleotide comprising a contiguous stretch of at least about 30 nucleotides of at least one of SEQ ID NOS:9, 10, 12, 13, 17, and 18.

3. (Three Times Amended) An isolated polynucleotide comprising a contiguous stretch of at least about 60 nucleotides of at least one of SEQ ID NOS:9, 10, 12, 13, 14, and 16-18.

4. (Amended) An isolated polynucleotide according to Claim 3, wherein said polynucleotide sequence comprising at least one of SEQ ID NOS:9-18.

10. (Twice Amended) An oligonucleotide comprising a contiguous stretch of at least about 20 nucleotides of SEQ ID NO:16.

12. (New) An isolated polynucleotide consisting essentially of a contiguous stretch of at least about 125 nucleotides of SEQ ID NO:11 or 15.